REMARKS/ARGUMENTS

I. STATUS OF THE CLAIMS

Upon entry of this amendment, claims 25-26 and 29-36 will be pending in this application and are presented for examination. Claims 1-24 and 27-28 have been canceled without prejudice to future prosecution.

Claims 25, 26, 29, and 32-34 have been amended to add a colon at the end of the claim preamble. As such, no new matter has been introduced. Reconsideration is respectfully requested.

II. EXAMINER INTERVIEW

Applicants thank Examiners Rooney and Haddad for the in-person interview conducted on November 17, 2008, in which the pending claims, the present rejections, and the cited art were discussed. During the interview, the Examiners agreed to withdraw the present new matter rejection with regard to whether Applicants are entitled to the filing date of their priority document, U.S. Application No. 10/413,501 ("the '501 application"). The Examiners further agreed to consider Applicants' submission of arguments with respect to the cited art as a means to overcome the present rejection under 35 U.S.C. § 103(a).

III. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 25-26 and 29-36 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. Applicants respectfully disagree.

As discussed during the in-person interview, the Examiner's allegation that the '501 application fails to provide support for the instant claims is not an issue of whether the instant claims constitute new matter, but whether Applicants are entitled to the filing date of the '501 application. In fact, the Examiner does not contend that the instant specification lacks support for the instant claims. Rather, the Examiner's position is that the instant claims recite limitations that are not disclosed in the '501 application.

Applicants acknowledge with appreciation that the Examiner has agreed to withdraw the present rejection and address whether Applicants are entitled to the filing date of the '501 application as an issue of priority instead of new matter.

In view of the foregoing, Applicants respectfully request withdrawal of the present rejection under 35 U.S.C. § 112, first paragraph.

IV. REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claims 25-26 and 29-31 under 35 U.S.C. § 103(a) as allegedly being obvious over Targan *et al.* in view of Vasiliauskas *et al.* and Landers *et al.* In response, Applicants respectfully traverse the rejection.

A claim is considered obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in *Graham*. The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. § 103 should be made explicit. One of the rationales addressed by the court in *KSR* supports a finding of obviousness when the prior art reference (or combination of references): (1) teaches or suggests the claim elements; (2) provides some suggestion or motivation to combine the references; and (3) provides a reasonable expectation of success. M.P.E.P. § 2143.

The Examiner alleges that Targan *et al.* is being relied on simply for its teaching that a subset of Crohn's disease patients has the serological markers I2 and OmpC. With respect to Vasiliauskas *et al.*, the Examiner states that this reference teaches detecting ASCA and ANCA antibodies as a tool to stratify Crohn's disease into immunologically homogenous subgroups with distinct characteristics including fibrostenosis, internal perforating disease, and the need for

small bowel surgery. The Examiner is of the opinion that one of ordinary skill in the art at the time of invention would have combined the OmpC and I2 markers with ASCA to further stratify the fibrostenotic subgroups, especially given the fact that some types of Crohn's disease are associated with other bacterial markers as taught by Targan *et al.* and Landers *et al.*

Applicants assert that Vasiliauskas *et al.* merely teach the use of ASCA and ANCA in stratifying Crohn's disease in patients. There is certainly no mention of anti-I2 antibodies or anti-OmpC antibodies and their use in combination with ASCA to assess the risk of having or developing various Crohn's disease subtypes. In fact, Vasiliauskas *et al.* ***teach away*** from the presently claimed methods by disclosing that ***all*** patients with high levels of ASCA without ANCA developed fibrostenosis, with the vast majority experiencing internal penetrating complications (79%) and the need for small bowel surgery (86%). *See,* page 492, right column and Figures 2-3. As a result, one of ordinary skill in the art would not have sought additional markers to stratify Crohn's disease into the instantly claimed clinical subtypes because Vasiliauskas *et al.* explicitly teach that high levels of ASCA were independently associated with the universal occurrence of fibrostenosis, the frequent development of internal penetrating complications, and the significantly higher need for small bowel surgery in patients without ANCA. Given the teachings in Vasiliauskas *et al.* of the diagnostic power of using solely ASCA to stratify Crohn's disease into various clinical subtypes, one of ordinary skill in the art would have understood that it is neither necessary nor beneficial to include additional markers.

Even if one of ordinary skill in the art were motivated to stratify Crohn's disease using ASCA in combination with other markers, there is simply no teaching or suggestion in any of the cited references that ASCA should be specifically combined with ***both*** anti-I2 and anti-OmpC antibodies. Although Targan *et al.* teach the determination of ASCA, anti-I2 antibody, anti-OmpC antibody, and ANCA levels, there is no disclosure whatsoever that high levels of one or more of these markers are associated with any Crohn's disease subtypes. Absent such a teaching in Targan *et al.* that the levels of a particular combination of markers correlate with specific Crohn's disease subtypes, one skilled in the art could have easily chosen to measure ASCA levels in combination with ***either*** anti-I2 antibody or anti-OmpC antibody levels, or with

markers not described in the reference. As a result, Applicants assert that the Examiner has used impermissible hindsight to improperly combine specific markers taught by Targan *et al.* (anti-I2 and anti-OmpC antibodies) with a specific marker taught by Vasiliauskas *et al.* (ASCA) to arrive at the presently claimed methods. However, there is simply no rational underpinning to combine these references to support a legal conclusion of obviousness because Vasiliauskas *et al.* teach that ASCA alone is more than adequate in stratifying Crohn's disease, and Targan *et al.* fail to teach or suggest which specific marker(s) should be added to ASCA to stratify Crohn's disease if the skilled artisan were motivated to include additional markers.

Landers *et al.* does not supply the teachings that are clearly lacking in Targan *et al.* and Vasiliauskas *et al.* Rather, Landers *et al.* teach that serum immune responses to the microbial antigens ASCA, OmpC, and I2 and the autoantigen ANCA were not uniform among CD patients, but exhibited a diversity of patterns that differed widely among groups of CD patients. *See,* page 697, left column. In fact, Landers *et al.* ***teach away*** from the presently claimed methods by stating that "[t]he relationship of these different patterns of immune responses to clinical behavior is not yet clear." *See, id.* Therefore, one skilled in the art would appreciate that Landers *et al.* did not investigate, let alone identify, any associations between the different patterns of immune responses observed and specific Crohn's disease subtypes.

As with Targan *et al.*, absent such a teaching in Landers *et al.* that the levels of a particular combination of markers correlate with specific Crohn's disease subtypes, one skilled in the art could have easily chosen to measure ASCA levels as taught by Vasiliauskas *et al.* in combination with ***either*** anti-I2 antibody or anti-OmpC antibody levels, or with markers not disclosed in the reference. Again, Applicants assert that the Examiner has used impermissible hindsight to improperly combine specific markers taught by Targan *et al.* and Landers *et al.* (anti-I2 and anti-OmpC antibodies) with a specific marker taught by Vasiliauskas *et al.* (ASCA) to arrive at the claimed invention. However, there is simply no rational underpinning to combine these references to support a legal conclusion of obviousness because Vasiliauskas *et al.* teach that ASCA alone is more than adequate in stratifying Crohn's disease, and neither Targan *et al.*

nor Landers *et al.* teach or suggest which specific marker(s) should be added to ASCA to stratify Crohn's disease if the skilled artisan were motivated to include additional markers.

For the foregoing reasons, Applicants submit that the cited references, whether alone or in combination, fail to contemplate the presently claimed methods for determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease, or the need for small bowel surgery by determining the magnitude of three specific markers: anti-I2 antibodies, ASCA, ***and*** anti-OmpC antibodies.

Accordingly, Applicants respectfully request withdrawal of the present rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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